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| 09/076,956 | 05/13/98 | BARANOVA | L P60188US1 |

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HM22/1115

EXAMINER

CRANE, L

ART UNIT

PAPER NUMBER

1623

23

DATE MAILED:

11/15/00

Please find below and/or attached an Office communication concerning this application or proceeding.

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Office Action Summary

Application No.
09/076,956

Applicant(s)
Baranova ~~et~~ et al.

Examiner
L. E. Crane

Group Art Unit
1623

—The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address—

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE ---3--- MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

- ☒ Responsive to communication(s) filed on September 5, 2000 (Amdt F)-----
- ☒ This action is **FINAL**.
- ☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

- ☒ Claim(s) 104-107-----is/are pending in the application.
- Of the above claim(s)----- is/are withdrawn from consideration.
- ☐ Claim(s)----- is/are allowed.
- ☒ Claim(s) 104-107-----is/are rejected.
- ☐ Claim(s)----- is/are objected to.
- ☐ Claim(s)----- are subject to restriction or election requirement.
- ☒ Claims 80-103 have been cancelled.

Application Papers

- ☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
- ☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
- ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
- ☐ The specification is objected to by the Examiner.
- ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119 (a)-(d)

- ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- ☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been received.
- ☐ received in Application No. (Series Code/Serial Number) _____.
- ☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

Attachment(s)

- ☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____
- ☐ Interview Summary, PTO-413
- ☐ Notice of Reference(s) Cited, PTO-892
- ☐ Notice of Informal Patent Application, PTO-152
- ☐ Notice of Draftsperson's Patent Drawing Review, PTO-948
- ☐ Other _____

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The Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group 1600, Art Unit 1623.

- 5 Claims **80-103** have been cancelled and new claims **104-107** have been entered as per the amendment of September 5, 2000.

Claims **104-107** remain in the case.

The disclosure is objected to because of the following informalities:

- 10 The schemes at pp. 20-22, particularly Scheme 4, include chemical formulas which are are not entirely legible, in some cases include lines which suggest valence errors (trivalent oxygen, etc.), and in some cases do not include substituents which should not have disappeared via the chemical process steps specified (look for missing -OR₃ at the end of scheme 4, etc.). Substitution of clearly drawn schemes is respectfully
15 requested.

Appropriate correction is required.

Claims **104-107** are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

- 20 In claims **104-107**, line 4, the term "X is an alkyl radical" is technically incorrect. Did applicant intend the term to read -- X is an alkylenyl diradical -- (where alkylenyl diradical has the chemical formula -(CH₂)_x-)? In addition, the attachment point for the "X" substituent is highly unusual in oligonucleotide synthesis in addition to

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being inconsistent with the disclosure at pp. 11-12 (see enablement rejection below).

Applicant's arguments with respect to claims **80-103** have been considered but are deemed to be moot in view of the new grounds of rejection.

In claims **104-107**, lines 3 and 5, the attached substituent "Y" at the "CH₂-O-" location defined as "a purine or pyrimidine base," is incomplete because the structural attachment point of the purine or pyrimidine is not defined and suggests a very serious technical error because the noted "CH₂-O-" location is almost always the site used to attach the oligonucleotide chain being synthesized; e.g. a specific nucleoside 3'-phosphoramidite reagent reacts with the 5'-hydroxyl to form a 3'->5' phosphite diester linkage, etc. ala the Caruthers et al. protocol. The instant claimed structures are also inconsistent with the disclosure at pp. 11-12 wherein the "CH₂-O-" location remains open for oligonucleotide chain attachment/synthesis (see the enablement rejection below).

Applicant's arguments with respect to claims **80-103** have been considered but are deemed to be moot in view of the new grounds of rejection.

In claims **104-107**, line 5, the term "purine or pyrimidine base" incorrectly refers to classes of compounds. Did applicant intend the term to read -- purinyl or pyrimidinyl base --?

Applicant's arguments with respect to claims **80-103** have been considered but are deemed to be moot in view of the new grounds of rejection.

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Claims **104-107** are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

In claims **104-107**, at line 3, chemical formulas are presented which show a bond directly between the 2- or 3-carbon of a ribose moiety and the linker moiety "X" which provides an anchor to the solid "Support." Making particular reference to the Schemes at pp. 20-22 of the instant disclosure suggests that none of the chemical formulas provided within the instant claims is enabled in any way by the exemplifications of the disclosure. Therefore, the instant disclosure fails to provide an adequately supportive written description which would permit the ordinary practitioner to practice the synthesis of, or the use of, the materials claimed herein.

Applicant's arguments with respect to claims **80-103** have been considered but are deemed to be moot in view of the new grounds of rejection.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. §102 that form the basis for the rejections under this section made in this Office action:

"A person shall be entitled to a patent unless -

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent."

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(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States."

5 Claims **104-107** are rejected under 35 U.S.C. §102(a) as being anticipated by Lyttle et al. (PTO-892 ref S). (See also the US patent equivalent 5,688,940, PTO-892 ref. H).

10 The instant claims are directed to compounds which include an oligonucleotide cleavage capable nucleophilic function "Y" and its protected precursor "Y-W" which are deemed to read on one or more of the compounds numbered 1, 4 and 5 as disclosed in the Lyttle et al. reference at Fig. 1, col. 1, of p. 2795, and particularly to read on the first structure of Figure 2 at column 1 of page 2796.

 Applicant's arguments filed September 9, 2000 have been fully considered but they are not deemed to be persuasive.

15 The above rejection and the following rejections have been repeated based on the presumption that applicant may elect to claim subject matter actually enabled herein. Applicant is requested to carefully compare the instant cited art to the instant disclosures (e.g. Schemes 1-4 at pp. 20-22) before amending claims.

20 Claims **104-107** are rejected under 35 U.S.C. §102(b) as being anticipated by Nelson et al. (PTO-892 ref. Y).

25 Applicant is referred to p. 7188, Figure 1 wherein the structure labeled "MF-CPG" (final product) anticipates previous claims 90-96. The associated text at pp. 7187-7188 which teaches attachment of a growing nucleotide in place of the DMT group thereby anticipates previous claims 99-103.

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Applicant's arguments filed September 9, 2000 have been fully considered but they are not deemed to be persuasive.

See examiner's comments in response following the first art rejection.

5 Claims **104-107** are rejected under 35 U.S.C. §102(b) as being anticipated by Vu et al. (PTO-892 ref. **V**).

10 Applicant is referred to p. 604, Figure 1, the compounds labeled with numbers **5, 6, 13, 19, 26 and 32**, each of which anticipate applicant's invention. Applicant will note with the abstract discussion to the effect that the phthalimido protecting group was inserted herein to prevent "spontaneous cleavage" of the oligonucleotides from the solid support.

Applicant's arguments filed September 9, 2000 have been fully considered but they are not deemed to be persuasive.

See examiner's comments in response following the first art rejection.

15 The following is a quotation of 35 U.S.C. §103(a) which forms the basis for all obviousness rejections set forth in this Office action:

20 "A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made."

25 Claims **104-107** are rejected under 35 U.S.C. §103(a) as being unpatentable over Lyttle et al. (PTO-892 ref **S**). (See also the US patent equivalent 5,688,940, PTO-892 ref. **H**).

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The instant claims are directed to the invention encompassed by previous claims 90-96 and 99-103 with the only differences being the presence of a cyclic structural element, optionally a heterocyclic ring, and further optionally a ribosyl moiety incorporating "C₁" and "C₂" as 2'- and 3'- ribosyl ring carbons, respectively, and the presence of optional alternative protected hydroxyl, protected N-alkylamino, or protected thio in place of protected amino as the protected reactive functional group "W-Y."

Lyttle et al. reference at Fig. 1, col. 1, of p. 2795 discloses derivatized solid supports which read on the instant claimed derivatized solid supports as noted supra. The instant reference does not include, i) N-alkyl analogues and ii) embodiments wherein the protected amino function and the solid support are connected by a moiety containing a cyclic structure which serves only a connecting function.

The disclosure in the prior art of a derivatized solid support which contains all of the chemically necessary structural and reactive elements of the instant invention, but does not contain a ring-forming structural element which serves only a connecting function and does not optionally include a protected hydroxyl group, a protected N-alkylated amino group or a protected thio group as the protected reactive group, is deemed to render the instant claimed derivatized solid support prima facie obvious in the absence of a showing of unexpected results associated with the presence of the cyclic connecting element and/or the alternative reactive functional groups.

Therefore, the instant claimed ring containing derivatized solid supports useful in oligonucleotide synthesis and solid support separation would have been obvious to one of ordinary skill in the art having the above cited references before him at the time the invention was made.

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In view of the disclosure of Vu et al. concerning unanticipated cleavage of ODN's from the solid support, both the Vu and Nelson references are deemed to be equivalents of the Lyttle reference. Therefore, this paragraph is considered to be the equivalent of obviousness
5 rejections citing the relevant portions of Vu and Nelson in place of Lyttle in the rejection supra.

Applicant's arguments filed September 9, 2000 have been fully considered but they are not deemed to be persuasive.

See examiner's comments in response following the first art rejection.

10 Applicant's amendment necessitated the new grounds of rejection. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. §1.136(a).

15 A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH
20 SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. §1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

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Papers related to this application may be submitted to Group 1600 via facsimile transmission(FAX). The transmission of such papers must conform with the notice published in the Official Gazette (1096 OG 30, November 15, 1989). The telephone numbers for the FAX machines
5 operated by Group 1600 are **(703) 308-4556** and **703-305-3592**.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner L. E. Crane whose telephone number is **703-308-4639**. The examiner can normally be reached between 9:30 AM and 5:00 PM, Monday through Friday.

10 If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. Gary Geist, can be reached at (703)-308-1701.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is **703-308-1235**.

15 LECrane:lec
11/13/00



GARY GEIST
SUPERVISORY PATENT EXAMINER
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